Synthesis of Organic Rigid Rod Linker Using Biomolecular Recognition Strategies

Senior Thesis

Presented in Partial Fulfillment of the Requirements for Graduation with Distinction in Chemistry in the Undergraduate College of Mathematical and Physical Sciences of The Ohio State University

By

Ling-Fung Kho

The Ohio State University

March 2006

Project advisor: Professor Dennis T. Bong, Department of Chemistry

Abstract

Research directed towards the synthesis of linearly conjugated oligomers (rigid rod linker) with functionalized side chains is described. The strategy is based on bromine-iodide selectivity of the Pd-catalyzed alkyne-aryl-coupling, triisopropylsilyl (TIPS) and trimethylsilyl (TMS) as an acetylene protecting group. Further derivation of the monomers to amides is described. Also, the synthesis of key intermediates has been achieved. The compounds are characterized by ^{1}H spectroscopy.

ACKNOWLEDGEMENTS

Dr. Dennis Bong, for offering the opportunity and taking the risk to let me work in his laboratory

Dr. RajanBabu, for his teaching in organic chemistry laboratory course, which motivate me to pursue an undergraduate research in the organic chemistry division; his input in the proposal; his guidance and advice for further education and future career

Dr. Zita Divis and Dr. Jovica Badjic, for attending my oral defense and their input

Yumei Luo, Mingming Ma, Yun Gong, for their support and motivation, especially Yumei Luo and Mingming Ma for answering massive questions about mechanisms and synthesis throughout the project

Mrs. Loo, for spurring my interest in Chemistry during the early days of my education and believing in me; who I have been deeply in gratitude

Andrew Browne, for his passion in academic research which inspires me to consider the possibility of a career in academic research

Cykay Kho, my brother, for taking care of my general well-being

Joline Kho, my sister, for her awefully witty jokes and making my laughter louder than the croaking of the frog

Kim and Douglas Sherman, for having been here through thick and thin

Mom and Dad, for their love and parental support throughout life

All other lab members, Matt Bernadina, Oscar Torres, Mathilde Gifard and my friends, Mary Vade-Bon-Couer, Carla Marcelo, Jeannette Vazquez, for their support throughout the project and friendships

TABLE OF CONTENTS

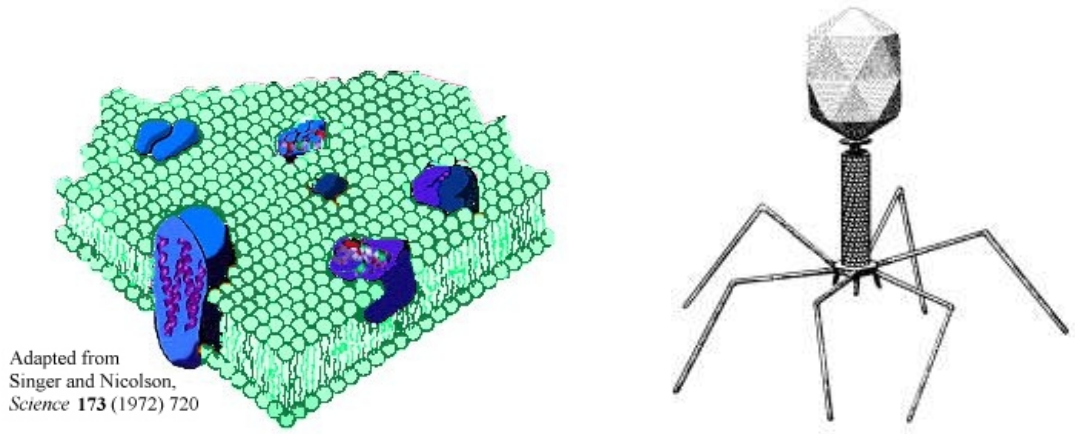
Chapter 1

Introduction

Self-Assembly

Self assembly, a field originates in organic chemistry is an autonomous organization of components into patterns or structures without human intervention. It is also described as the creation of material from its constituent components in a spontaneous, 'natural' manner, i.e. by an interaction between the components or by a specific rearrangement of them, that proceeds naturally without any special external impetus.[1] Also known as 'Brownian assembly'. A typical example are self-assembled monolayers where molecules spontaneously form an extremely well ordered layer only one molecule thick when deposited on substrates (e.g. Au (gold)). Another example is a self-assembly of proteins in protein structures (in cells) such as microtubules, actin filaments and similar. Although individual proteins stochastically move within a cell (Brownian motion), they eventually stick to a specific place as a properly positioned part of an ordered structure. This term is not related to self-assembler (or assembler) which is a speculative nano-fiction concept (nanobot).[1] Molecular self-assembly is a strategy for nanofabrication that involves designing molecules and supramolecular entities so that shape-complementarity causes them to aggregate into desired structures. Self-assembly has a number of advantages as a strategy: First, it carries out many of the most difficult steps in nanofabrication--those involving atomic-level modification of structure--using the very highly developed techniques of synthetic chemistry. Second, it draws from the enormous wealth of examples in biology for inspiration: self-assembly is one of the most important strategies used in biology for the development of complex, functional structures[5]. Third, it can

incorporate biological structures directly as components in the final systems. Fourth, because it requires that the target structures be the thermodynamically most stable ones open to the system, it tends to produce structures that are relatively defect-free and self-healing. However, self-assembly also poses a number of substantial intellectual challenges. There challenges are that we do not yet know how to do it, and cannot even mimic those processes known to occur in biological systems at other than quite elementary levels. Although there are countless examples of self-assembly all around us--from molecular crystals to mammals--the basic rules that govern these assemblies are not understood in useful detail, and self-assembling processes cannot, in general, be designed and carried out "to order". Many of the ideas that are crucial to the development of this area--"molecular shape", the interplay between enthalpy and entropy, the nature of non-covalent forces that connect the particles in self-assembled molecular aggregates--are simply not yet under the full control of investigators.



(a) (b)

Figure 1: Examples of biological self assembly: (a) biological cell membrane, (b) bacteriophage

In addition, there are issues of function in self-assembled aggregates that need solution. The most promising avenues for self-assembly are presently those based on organic compounds, and organic compounds, as a group, are electrical insulators; thus, many ideas for information processing and electrical/mechanical transduction will require either fundamental redesign in going from the macroscopic systems presently used to self-assembled systems, or the development of new types of organic molecules that show appropriate properties[6].

One of the approaches to self-assembled structures that have been particularly successful: is self-assembly on surfaces.[5-6] There are now a range of different molecular systems that self-assemble--that is, form ordered, monomolecular structures--by the coordination of molecules to surfaces. These systems--self-assembled monolayers (SAMs)--are reasonably well understood, and increasingly useful technologically. The crucial dimension in SAMs is the thickness perpendicular to the plane of the monolayer: this dimension, and the componsition along this axis, can be controlled very simply at the scale of 0.1 nm by controlling the structures of the molecules making up the monolayer. SAMs also provide tailorable functions: for example, by changing the structures of the organic molecules in straightforward ways, interfacial free energies can be controlled.[6] Complementary techniques such as microcontact printing (uCP) allow the in-plane dimensions of structures in SAMs to be controlled easily at the scale of 500 nm, and with difficulty at smaller dimensions.[5-6] SAMs represent one type of structure that is using molecular self-assembly to build structure and function on the nanometer scale. They are

not a general solution to the problem of building functional nanostructures, but the lessons learned from them will be valuable in building more versatile systems. They also are among the first of the self-assembled systems to move into technology, and there are lessons that can be learned from them about technology transfer and nanotechnology.

As mentioned above, self-assembling processes are common throughout nature and technology. It is widely applied in synthesis and fabrication and used in crystallization at all scales, robotic and manufacturing, bottom up or top-down approaches in nanoscience, chemical synthesis for nanostructures, microelectronic and netted systems in computers, sensors and controllers. Microelectronic which is based on photolithography-an intrinsically two dimensional technology- is nearing its limits. The top to bottom approach in lithography does not seem to scale the microelectronic devices smaller than it has been.[1] Biomimetic self-assembly, which is a bottom-top approach would logically bridge lithographic limits and natural nanoscale organization, allowing highly functionalized materials ordered at length scales previously unexplored. Chemical synthesis is developing a range of methods for making nanostructures such as nanotubes, wires and colloids, to use in bottom-up approaches. Self assembly offers a route for assembling these components into larger functional ensembles[3], such as the conjugated oligomers.

Conjugated Oligomers

Conjugated oligomers are polymers linked by carbon-carbon triple bond. There are two known types of conjugated oligomers, the linearly conjugated and the cross-conjugated oligomers (figure 2).

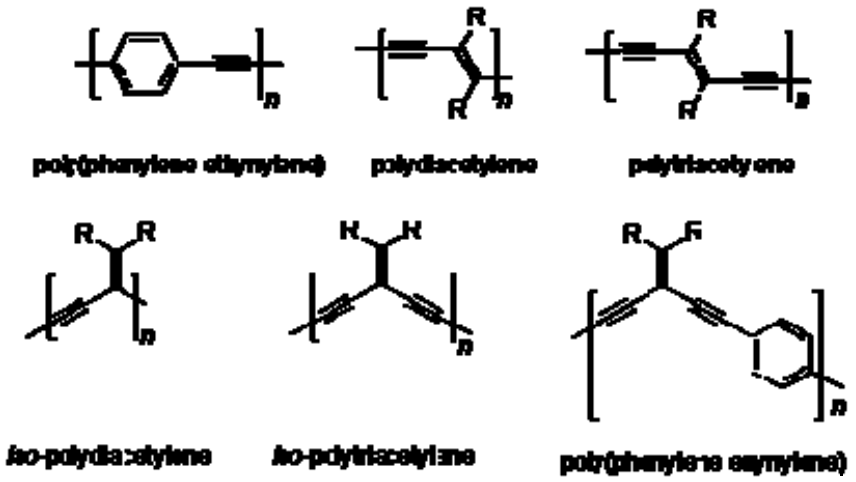


Figure 2: Linear and cross-conjugated oligomers.

The preparation of conjugated molecules of defined length and constitution is vital for the realization of both molecules and polymers suitable for use as materials for molecular-scale electronics, organic luminescent devices, and nonlinear optical (NLO) media.[4] The ability to tailor organic molecular structure using organic synthetic techniques provides great versatility to modulate the properties of these molecules toward various applications. Conjugated oligomers of precise length and constitution have received considerable attention both as models for analogous bulk polymers and as candidates for molecular wires and molecular scale electronic devices.[3] Shape persistent oligophenyleneethynylenes (OPEs) appear especially attractive for their excellent main-chain rigidity and interesting electronic characteristics. [4] Several synthetic methods including solution and solid phase synthesis have been reported for preparing oligophenyleneethynylenes.[5-6] In most of the reported methods, isolation of air unstable terminal alkyne or bis(terminal alkynes) is necessary.

This synthesis synthesized two dimensional organic frameworks using Pd/Cu-catalysis, also known as the Sonogashira coupling and biomolecular recognition strategies, which allow precise placement and definition of chemical functionality on the nanoscale.

Cross Coupling Reaction to sp Carbon Atoms

Alkyne cross coupling reactions have seen incredible growth over the past quarter century, proving their worth as an important tool for organic synthesis. The rigidity and electron-rich nature of the alkyne moiety are not only structurally appealing but also provide a point of unsaturation for further derivatization and/or transformation. One of the most important synthetic advancements have been the utilization of palladium (Pd) as a catalyst. Pd is currently favored in the vast majority of sp cross-couplings. The Pd-catalyzed reaction of a terminal alkyne with its coupling partner in the presence of a Cu co-catalyst an amine base is the most widely used cross-coupling technique and is known as the Sonogashira coupling.

Sonogashira Coupling

Generation of Pd(0) from Pd(II) proceeds via transmetallation of an alkynyl copper, which is generated by the reaction of the amine base and CuI, followed by reductive elimination of the dialkynylPd(II) species (a) to give species (b) and 1,3-butadiyne (c). Compund (c) which is formed by the reduction of the Pd(II) complex, is also a common by product that plagues Sonogashira reactions, and sometimes is the major acetylene containing product. Although this dimerization is often detected even when Pd(0) catalyst is used it can be minimized by the careful purging of oxygen from the solvents and by

running the reaction under an inert atmosphere. Upon formation of the active Pd(0) catalyst (b), oxidative addition of the aryl or vinyl halide occurs providing Pd(II) complex (d). This step is critical for the catalytic process, and a number of new catalysts have been designed for its enhancement. Transmetallation with the Cu-acetylide next gives (e) and finally reductive elimination follows to afford the cross coupled product as well as to regenerate the active catalyst. There are many variables that dictate the overall efficiency of the catalytic cycle, including ligands, amine base, copper salt, solvent, other additives and the electronic and steric characteristics pf the organic electrophile and alkyne. Electron deficient organ0halides are again more reactive to cross coupling than electron-rich while the apposite is true for the alkyne. The general reactivity order of the sp^2 species is vinyl iodide > vinyl triflate > vinyl bromide > vinyl chloride > aryl iodide > aryl triflate > aryl bromide >> aryl chloride.

Amine Bases

The amine base is another crucial element of the Sonogashira reaction. Et_3N, Et_2NH, iPr_2NH are the most widely used bases and show good results in most circumstances although success can be highly substrate dependent. It has been reported that stronger bases considerably increase yield and reaction rate when no CuI co-catalyzed is used in the reaction(10). Another study describes the reaction rate decreasing in the order of $BuNH_2$>Et_3N>iPr_2NH>Et_2NH>K_2CO_3 for the cross coupling of trimethylsilylacetylene (TMSA) with iodopyridone (11).

Amine	Time	Yield
Et_3N	22 h	0
i-Pr_2NH	26 h	2
Et_2NH	24 h	0
$BuNH_2$	25 h	85
piperidine	6 h	76
pyrrolidine	2.5 h	93

Solvent and Additives

Sonogashira protocol indicates that the amine base functioned not only as a reactant but also as the solvent. However reaction rate and yield can be improved by using a mixture of amine with other solvents, most notably tetrahydrofuran (THF). With THF as co-solvent, yields typically higher than with only Et_3N and reactions are milder. No detailed explanation for the reaction improvement due to solvent effects, although in many cases an increase in the solubility of catalysts, reactants, and products seems to be the major factor.

Silane Protecting Groups

Trialkylsilanes are commonly used as protecting groups for terminal alkynes as many alkynylsilanes are commercially available trimethylsilylacetylene (TMSA) and triisopropylsilylacetylene (TIPSA). TMSA can easily be cross-coupled with haloarenes using the Sonogashira reaction and deprotected by treatment with aqueous or methanolic KOH or K_2CO_3 or with fluoride source such as KF, to give the terminal acetylene.

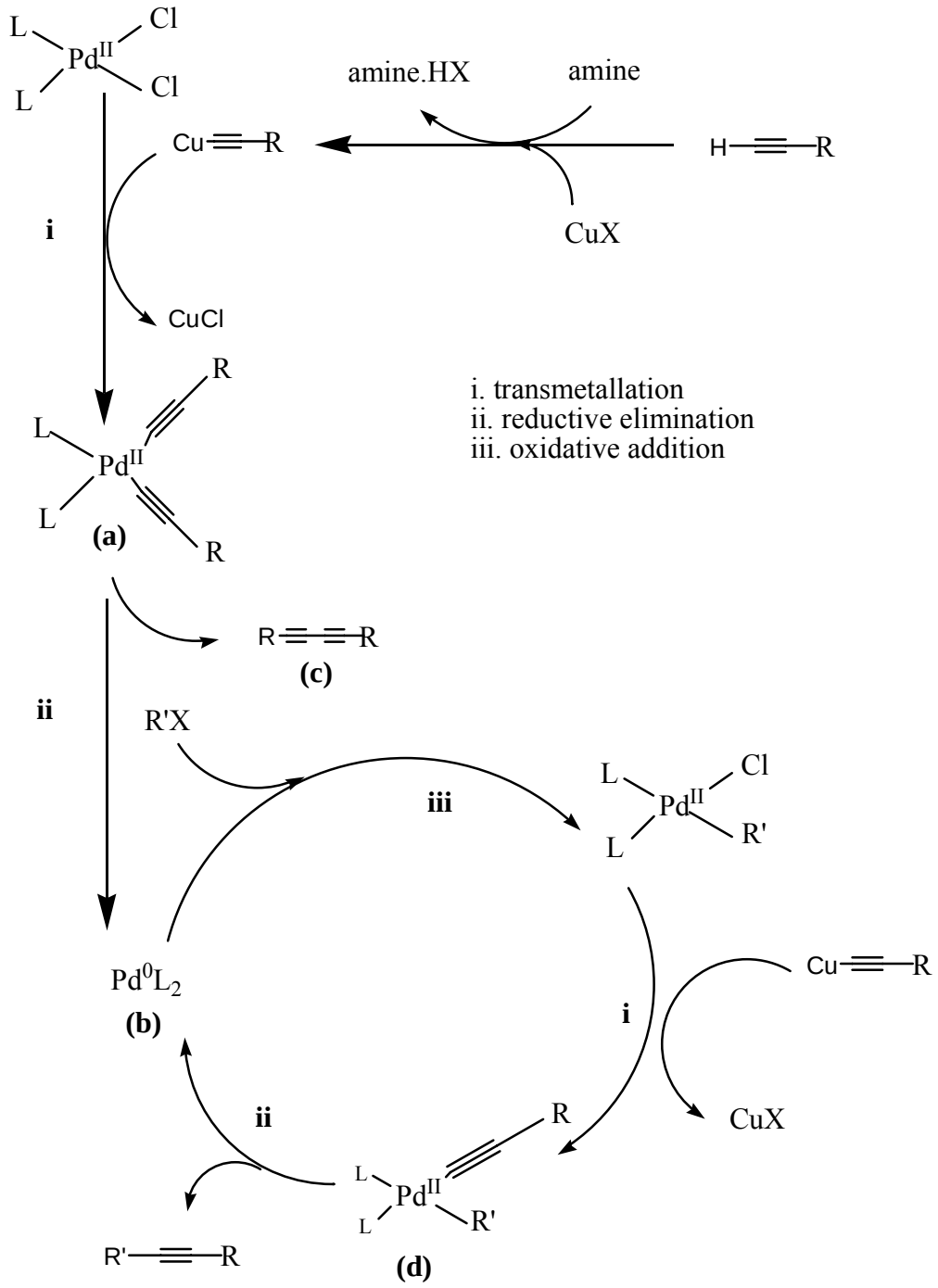


Figure 3: Pd/Cu catalyzed cross coupling

Proposed Synthesis

Nature uses protein ligand interaction as coupling reaction in the growth of biomaterials. However, the multivalent protein ligand binding is ideal for construction of biomaterials by designed non-covalent growth as it represents the natural union of synthetic structures such as small molecule ligands with biomolecular backbones such as the DNA. In this project, nanoscale ordered molecular arrays were to be constructed by coupling multivalent proteins with synthetic rigid-rod linkers functionalized at each end with protein ligands (figure 4).

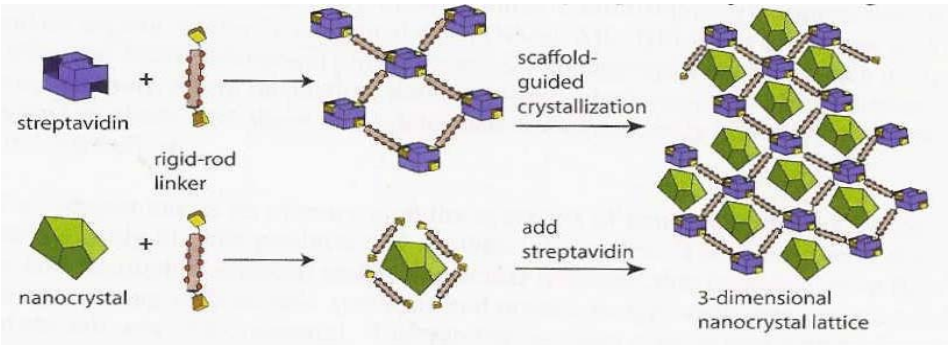
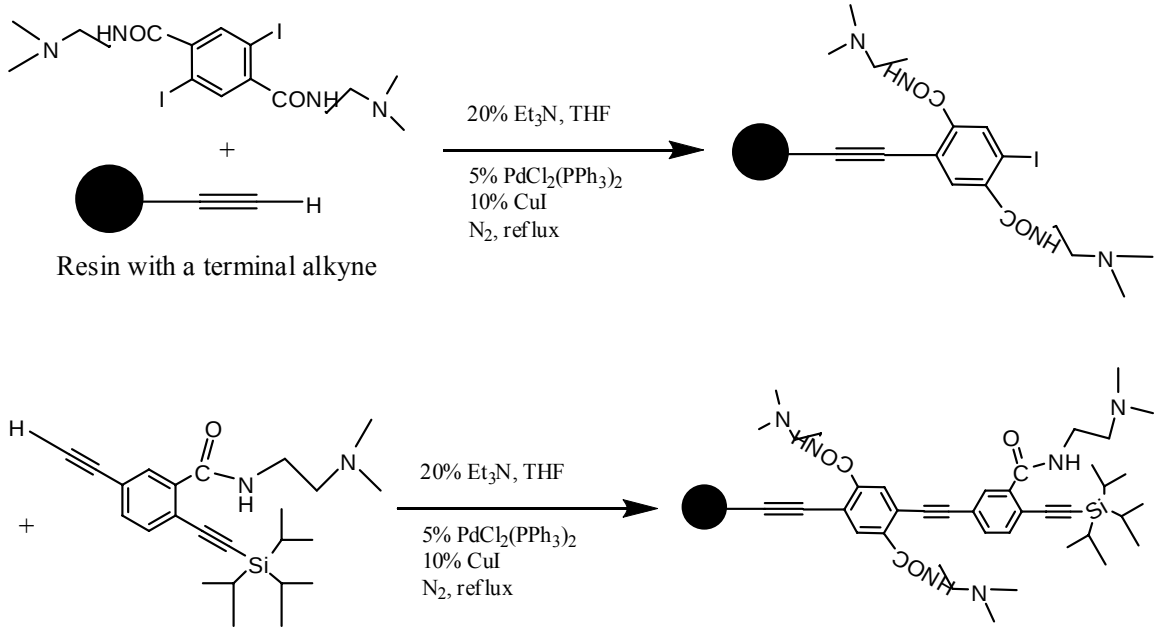


Figure 4: coupling multivalent proteins with synthetic rigid-rod linkers functionalized at each end with protein ligands.[10]

Construction is possible due to the fixed valency and geometry of protein ligand binding and the rigidity of appropriately designed synthetic modules. Streptavidin, a tetrahedral candidate for protein binds biotin (a ligand) with pseudo-tetrahedral symmetry, making it an ideal molecular hub to be linked with a rigid oligophenyleneethylene (OPE). Equilibration[7] is usually required to reach ordered structures. Self-assembly requires that the components either equilibrate between aggregated and non-aggregated states or adjust their positions relative to one another once in aggregate. Structure equilibration can be

reached by controlling the growth rate of the arrays using streptavidin mutants with attenuated biotin binding constants. These scaffolds could be tuned by synthesizing OPEs of varying length and substitution so that the chemical content and dimension of the nanocavities formed can be controlled. Moreover, these assemblies could be pinned to a surface and limited to two dimensional growth by incorporating surface chemisorbing groups such as thiols/ gold surfaces in some of the alkyl group along the OPE backbone (figure 1), yielding a two dimensional ordered template[8]. It is possible to obtain these rigid linkers and functionalize the with protein ligands. Streptavidin and biotin are available commercially. Streptavidin is a roughly 5-nm sphere and OPEs ranges from 5-10 nm long are accessible. These analytical tools were to be used to determine the crystalline structure of assembly and the template effect. The final component is shown in figure 5.



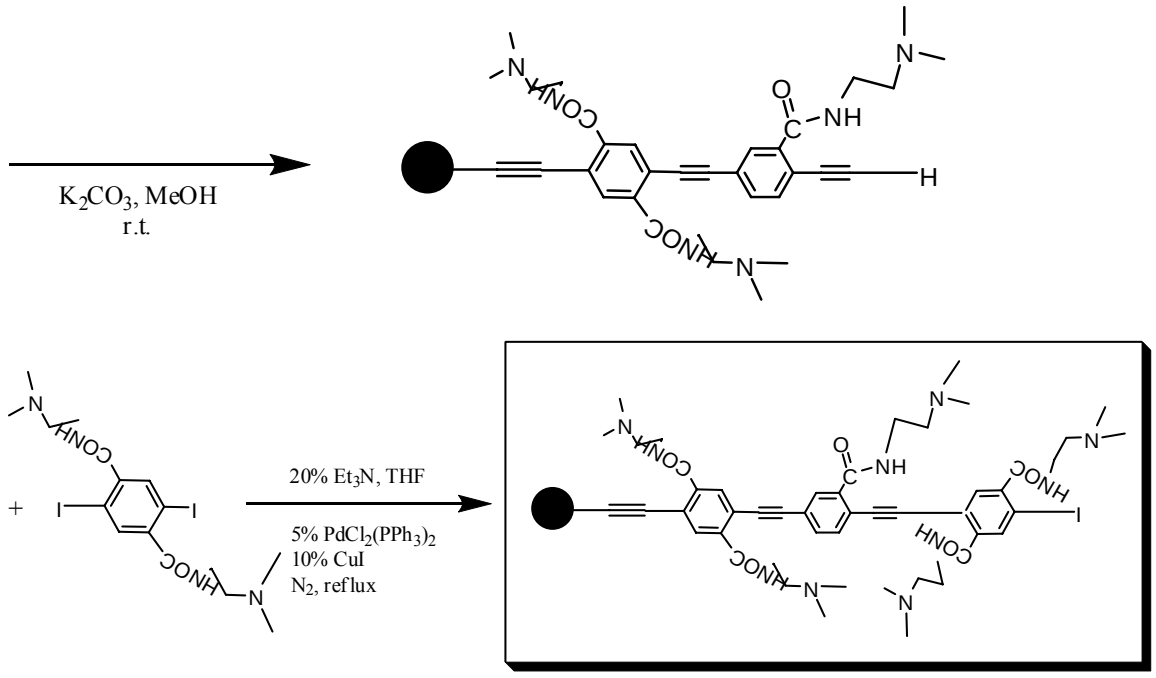
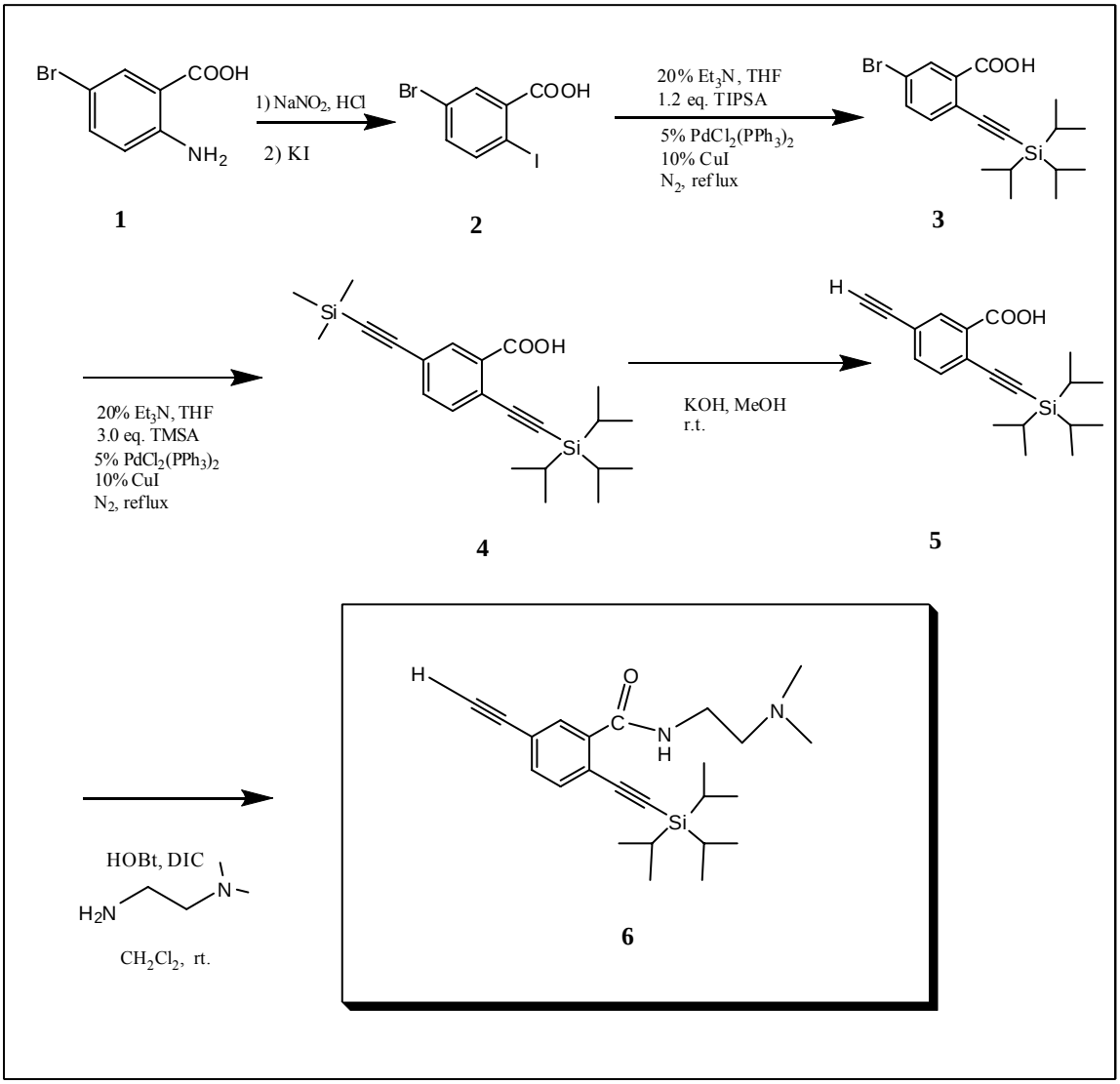


Figure 5: The desired oligomer is shown in the box. Oligomer is synthesized unit by unit to form a long chain of polymer.

Chapter 2

Results and Discussions

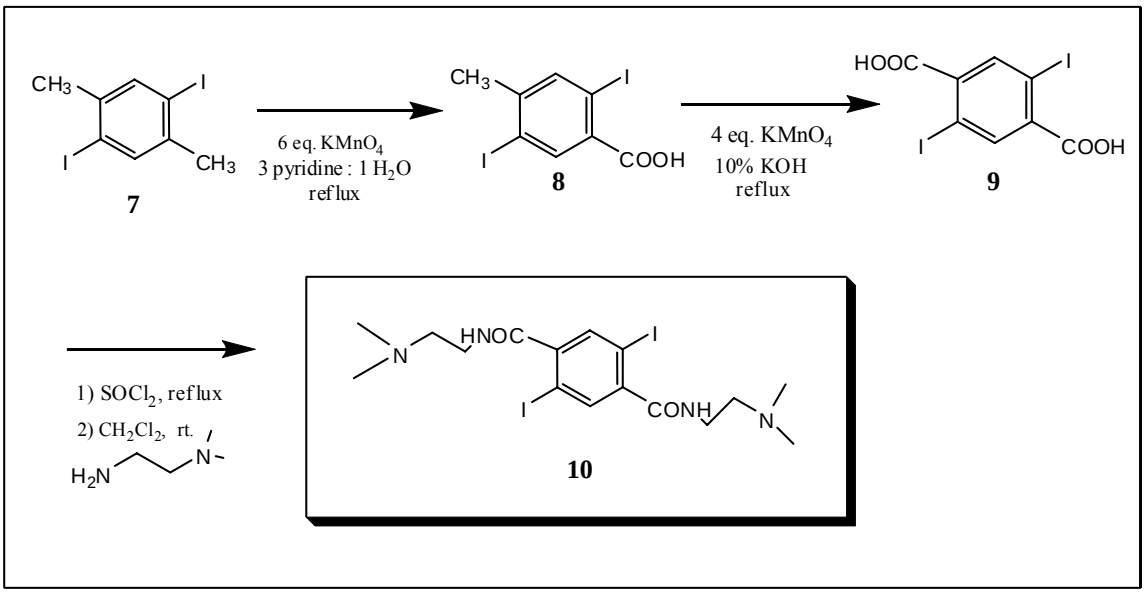
Part A: Submonomer Synthesis



The synthesis of the functionalized rod linker derivatives is depicted in Scheme 1. Based on previously reported procedures[3], reaction of 2-amino-5-bromobenzoic acid with sodium nitrite in acidic aqueous at 0 ˚C resulted in a diazo salt, which was subsequently iodinated by potassium iodide, yielded 2 in an overall yield of 68%. It was found during

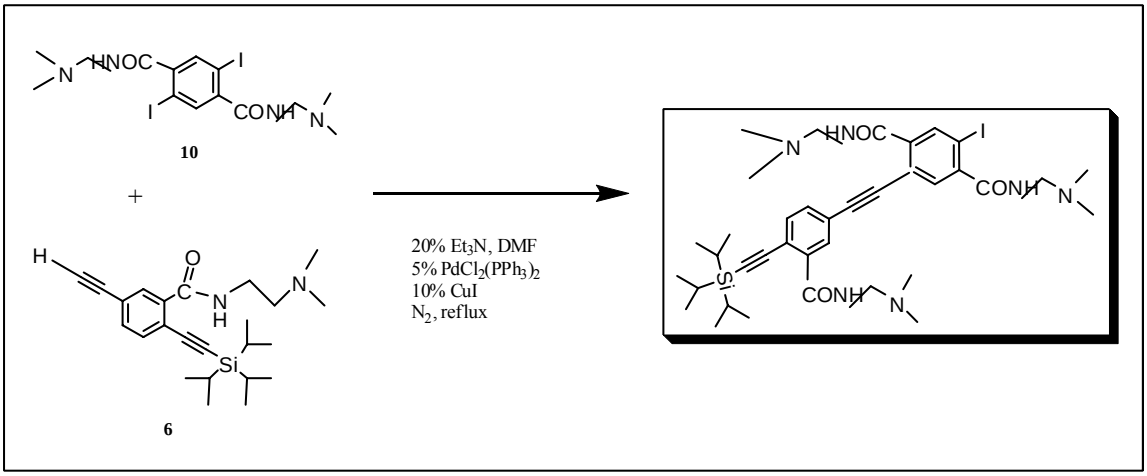
the work up that if the residue was not completely acidified before extraction using dichloromethane, a lot of emulsion would form at the organic layer. Based on the bromine-iodine selectivity of the Pd-catalyzed alkyne-aryl coupling, also known as Sonogashira-Hagihara coupling, the bromo-iodo compound 2 was cross coupled with triisopropylsilylacetylene (TIPS-acetylene) under Pd/Cu-catalysis yielding the monomer 3 in a yield of 76% after purification using column chromatography to separate byproducts of the cross coupling. Subsequently, 3 was coupled to trimethylsilylacetylene (TMS-acetylene) to give alkynylated compound 4 in 79% yield and then desilylation at room temperature using potassium hydroxide in methanol to afford air stable compound 4 in a good yield of 95%. Bisalkyne benzoyl chloride was formed by refluxing in an excess amount of thionyl chloride until no hydrochloric gas was formed. The intermediate was quickly reacted with N,N dimethylethylenediamine in dichloromethane at room temperature to afford an orange liquid of 81% yield.

Part B: Monomer Synthesis



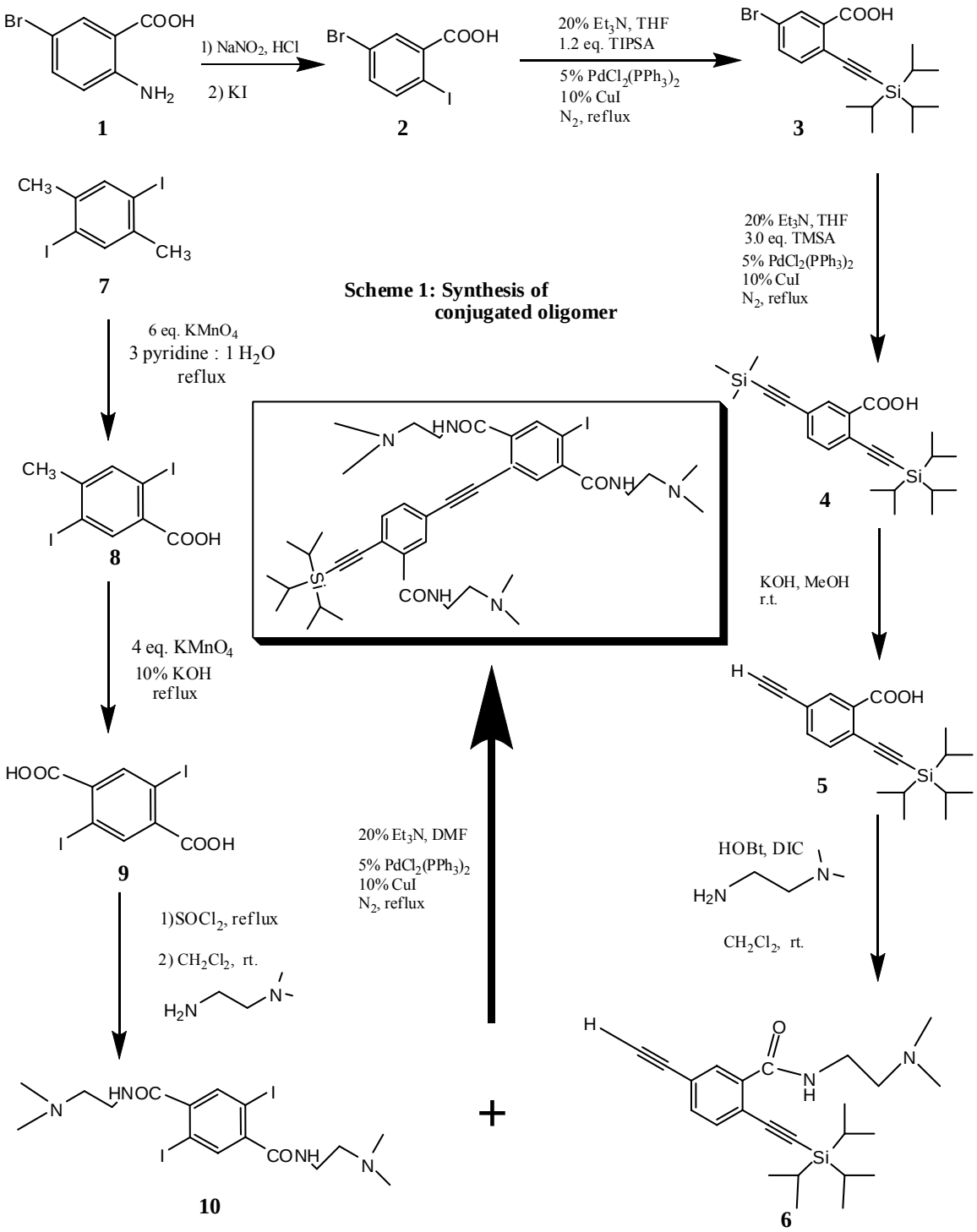
The efficient synthesis of monomer **10** required the oxidation of 2,6-diiodo-p-xylene by a two step procedure. A one step procedure gave very low yield. Following the procedures[9] , **7** was oxidized under mild basic conditions with 6 equivalent of potassium permanganate in 3 pyridine:1 water solvent, produced the monocarboxylate **8** with a 88% yield, which was readily isolated. The choice of pyridine as solvent was to maintain solubility throughout the reaction. The second oxidation step was then performed under strongly basic conditions with 4 equivalents of potassium permanganate in KOH/water to produce the dicarboxylic acid **9** in good yield of 88%. Simple acyl chlorination using excess thionyl chloride and subsequent amidation provides **10** with 86% yield.

Part C: Monomer Synthesis



To synthesize the desired monomer, one equivalent of **6** and one equivalent of **10** with Pd/Cu-catalyst, refluxed for 6 hours. Thin film chromatography showed the presence of **10** but **6** diminished. NMR results confirmed that **10** was unreacted. Experiment should

be repeated using different reagents or solvents under different conditions to find the optimum condition for reaction.



Scheme 1: Synthesis of conjugated oligomer

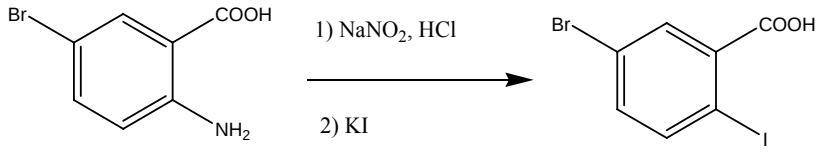
Chapter 3

Conclusions and Future Work

In conclusion, research directed towards the synthesis of conjugated oligomers has been presented. The diiodoterepthalamide moiety **10** and the alkynes **6** have been prepared and achieved. The coupling of **10** with **6** was unsuccessful partly due to non optimum reaction conditions and partly might be due to the bulky side chain which might have slowed the coupling process. Future work includes the coupling of **6** and **10** with optimized condition. The product of the successful coupling of **6** and **10** will be attached to a resin for templated growth or studies.

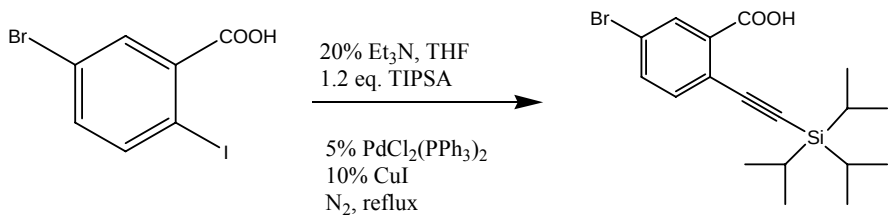
Chapter 4

Experimental



(1) **(2)**

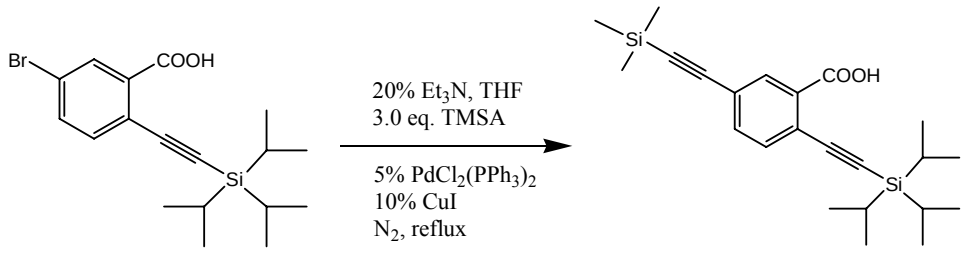
*5-bromo-2-iodo benzoic acid (**2**).* Sodium nitrite (13.16g, 190.7mmol) was dissolved in 20 mL water. In a 100 mL round bottom flask, potassium iodide (96.16g, 579.2mmol) was dissolved in 50 mL water. In a 500 mL round bottom flask, **1** (12.00g, 55.6 mmole) was added to a 25 mL concentrated hydrochloric acid until completely dissolved, stirred and cooled in ice bath at 0 ºC. The solution of sodium nitrite was added drop wise over 10 minutes. The mixture was let to stir for additional 20 minutes to form a brownish orange aqueous layer. The solution of potassium iodide was added to the mixture. Dark brown precipitation was observed with some foam on the surface of the solvent. The mixture was let to stir overnight. The mixture was worked up using concentrated sodium bisulfite to eliminate iodide anion in and gave a bright yellow solution. The solution was acidified to pH~1-2 and extracted using dichloromethane. Emulsion would be observed if the solution was not completely acidified. The organic layer was dried using a small amount of magnesium sulfate, filtered and concentrated under reduced pressure. The residue was recrystallized from ultra pure acidified water to yield **2** (11.74g, 68%) as a beige solid. ^{1}H NMR ($CDCl_3$, 250MHz): δ = 8.03(s, 1H), 7.82 (s, 1H), 7.24 (s, 1H).



(2) **(3)**

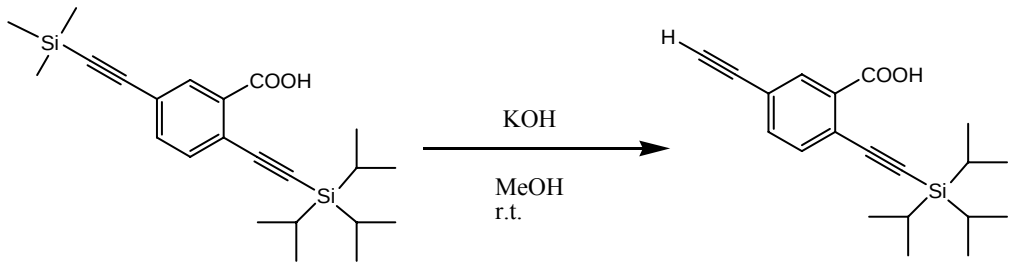
*5-bromo-2-[(triisopropylsilyl)ethynyl]benzoic acid (**3**)*. In a 250 mL round bottom flask, **2** (4.00g, 12.2mmole) dissolved in 125 mL 20% triethylamine in tetrahydrofuran was degassed vigorously with nitrogen. Triisopropylsilylacetylene (2.68g, 14.69 mmole), 5% dichlorobis(triphenylphosphine) palladium (II) (0.43g, 0.6mmole) and 10% copper(I) iodide (0.23g, 1.2 mmole) were added, stirred for 7 hours. The clear yellow solution turned cloudy yellow after 10 minutes. Formation of salt $Et_3N.HI$ was observed. The solvent was evaporated under reduced pressure, dissolved in dichloromethane and extracted using 1N hydrochloric acid. The residue was purified using column chromatography (99% 5 hexanes: 1 EtOAc, 1% acetic acid) to yield **3** (3.54g, 76%).

^1H NMR ($CDCl_3$, 250MHz): δ = 8.17(s, 1H), 7.62 (s, 1H), 7.47 (s, 1H), 1.1 (s, 21H)



(3) **(4)**

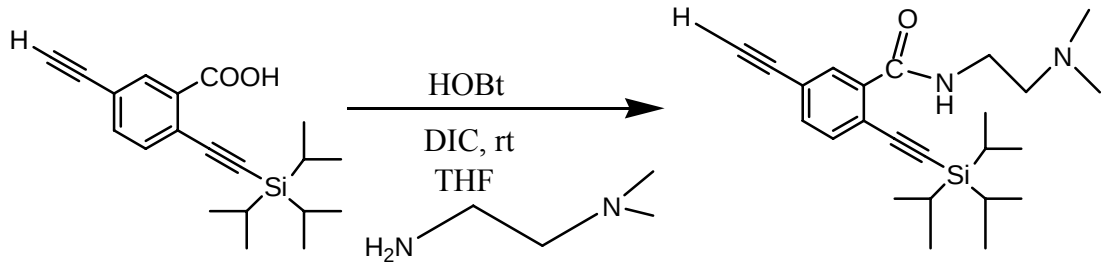
*2-[triisopropylsilyl(ethynyl)]-5-[trimethylsilyl(ethynyl)]benzoic acid(**4**)*. In a 100 mL round bottom flask, 3 (2.62g, 6.9mmole), trimethylsilylacetylene (2.02g, 20.6mmole), 5% dichlorobis(triphenylphosphine) palladium (II) (0.24g, 0.34mmole) and 10% copper(I) iodide (0.13g, 0.7 mmole) were added, stirred and refluxed for 6 hours. The completed reaction was worked up by evaporating the solvent under reduced pressure, redissolved in dichloromethane and extracted using 1N hydrochloric acid. The organic layer evaporated to dryness. The residue was purified by column chromatography (3 hexane: 2 EtOAc) to yield **4.** ^{1}H NMR ($CDCl_3$, 250MHz): δ = 8.05(s, 1H), 7.50(s, 1H), 7.40 (s, 1H), 2.05 (s, 9H), 1.0 (s, 21H).



(4) **(5)**

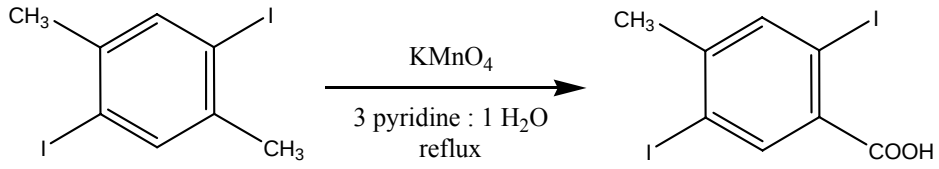
*2-ethynyl-5-[trimethyl(ethynyl)]benzoic acid (**5**).* In a 50 mL round bottom flask, 4 (0.11g, 0.3 mmole) was dissolved in 20 mL methanol. Potassium hydroxide (0.05g, 0.9 mmole) was added, stirred at room temperature until completion, followed by thin film chromatography. The solvent was evaporated; residue was redissolved in dichloromethane and extracted using 1 N hydrochloric acid. The organic layer was dried

using magnesium sulfate and evaporated under reduced pressure to yield **5** (0.09g, 98%). ^{1}H NMR ($CDCl_3$, 250MHz): δ = 8.10(s, 1H), 7.50(s, 2H), 3.10(s, 1H), 0.93 (s, 21H).



(5) **(6)**

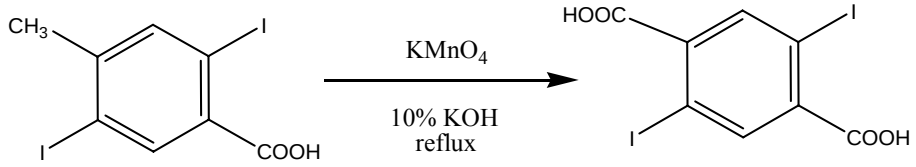
*2-ethynyl-5-[trimethyl(ethynyl)]terepthalamide(**6**)*. In a 50 ml round bottom flask, **5** (0.09g, 0.3 mmole) was dissolved in 20 ml of tetrahydrofuran with diiisopropylcarbodiimide DIC (0.08g, 0.6mmole) . HOBt (0.1g, 0.6mmole) dissolved completely in a small amount of tetrahydrofuran was added into the mixture, stirred overnight at room temperature. Solvent was evacuated, redissolved in dichloromethane, washed with sodium bicarbonate, brine and water. The organic layer was dried using magnesium sulfate. Solvent was evacuated to yield a light yellow liquid 6 (0.04g, 38%). ^{1}H NMR ($CDCl_3$, 250MHz): δ = 8.10(s, 1H), 7.50(s, 2H), 3.5 (q, 2H), 3.10(s, 1H), 2.52 (t, 2H), 2.26 (s, 6H), 0.93 (s, 21H).



(7) **(8)**

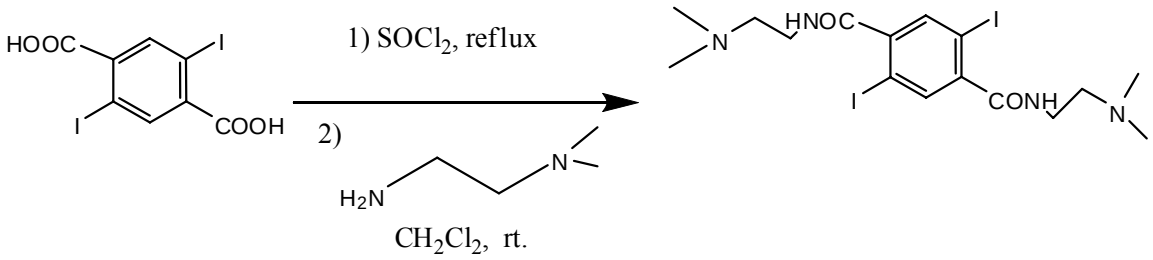
*4-methyl-2,5-diiodobenzoic acid (**9**)*. In a 500 mL round bottom flask, **7** (5.00g 14.0 mmole) was dissolved in 200 mL solvent (3 pyridine: 1 water). Potassium permanganate

(13.24 g, 84.0 mmole) was added. Mixture was stirred and refluxed for 6 hours. Initial purple solution turned brown after reflux. The mixture was filtered while hot and washed with 5% KOH which gives a clear filtrate. The filtrate was dried in vacuo to give white solid residue. The residue was redissolved in ultrapure water and acidified to pH < 1 using concentrated hydrochloric acid. Precipitation occurred, filtered and subjected to recrystallization using ethanol to yield **8** (4.77g, 88%). ^{1}H NMR (Methanol-d_4, 250MHz): δ = 8.27(s, 1H), 7.98(s, 1H), 2.42(s, 3H).



(8) **(9)**

*2,5-diiodo-1,4-dibenzoicacid (**9**)*. In a 500 ml round bottom flask, **8** (4.77g, 12.3 mmole) was added into a 200 mL 10% potassium hydroxide and potassium permanganate (7.76g, 49.2 mmole). The mixture was stirred to homogeneity, refluxed for 4 hours. The hot mixture was filtered. The left over solid was washed with 20 mL of hot 5% potassium hydroxide to form emerald green filtrate. The filtrate was evaporated to half of its original volume, acidified to pH <1 using concentrated hydrochloric acid, filtered to obtain off white solid. The solids were subjected to recrystallization using water to yield light yellow solid **9** (4.86g, 88%). ^{1}H NMR (Acetonel-d_6, 250MHz): δ = 8.37(s, 2H)



(9) **(10)**

*2,5-diiodo-1,4-terepthalamide (**12**).* **9** (1.00g, 2.4 mmole) and excess of thionyl chloride were combined and refluxed for 5 hours, after which no more HCl gas was evolved. Excess thionyl chloride was evacuated under reduced pressure. The residue was dissolved in dichloromethane and cooled to room temperature. The yellow liquid was reacted with 3 equivalent of N, N dimethyethylenediamine, let stirred at room temperature for 4 hours. The reaction mixture was washed with 1N HCl, water and brine. The organic phase was dried over magnesium sulfate and the solvent was removed under reduced pressure to afford **10** in 86% yield. ^{1}H NMR ($CDCl_3$, 250MHz): δ = 8.37(s, 2H), 3.5 (q, 4H), 2.52 (t, 4H), 2.26 (s, 12H)

Reference

[1] P. Ball, *The Self-Made Tapestry: Pattern Formation in Nature* (Oxford Univ. Press, Oxford, 1999).

[2] D. T. Bong, T. D. Clark, J. R. Granja, M. R. Ghadiri, in *Angew. Chem. Int. Ed*. 40, 988-1011 (2001).

[3] T. Gu, J. Nierengarten, in Tetrahedron Letters. **42**, 3175-3178 (2001).

[4] (a) Lunström, I., Salaneck, W. R., Ranby, B., Eds. *Conjugated Polymers and Related Materials. The Interconnection of Chemical and Electronic Structure*; Oxford University Press: Oxford, 1993. (b) Martin, R. E.; Diederich, F. *Angew. Chem. Int. Ed.* **1999**, *38*, 1350. (c) Müllen, K.; Wegner, G., Eds. *Electronic Materials: The Oligomer Approach*; Wiley-VCH: Weinheim, 1998.

[5] *The Use of Minimal Free Energy and Self-Assembly to Form Shapes*, Kim, E.; Whitesides, G.M., Chem. Mat. 1995, 7, 1257-12

[6] *Fabrication of Submicron Features on Curved Surfaces by Microcontact Printing* Jackman, R.; Wilbur, J.; Whitesides, G.M., Science, 1995, 269, 664-666

[7] L. Isaacs, D.N. Chin, N. Bowden, Y. Xia, G.M. Whitesides, in *Supramolecular Technology*, D.N. Reinhoudt, Ed. (Wiley, New York, 1999), pp. 1-46.

[8] N. Bowden, A. Terfort, J. Carbeck, G.M. Whitesides, in *Science*. **276** 233(1997).

[9] Zhou, Q., Swager, T. *J. Am. Chem . Soc*., Vol. 117, No. 50, 1995

[10] Dr Bong's Proposal